- 517) in view of Shinoda et al (Nippon Ishinkin Gakkai Zasshi, 1991, 32 Suppl.2 Proc. Annu. Meet. Jpn. Soc. Med. Mycol. 34th 1990, pages 83 - 93). Furthermore, claim 5 and 10 were rejected under 35 U.S.C. § 103(a) based on Hunter et al in view of Dosa et al further in view of Shinoda et al, and further in view of Nakase et al (JP 48019719 Abstract Only).

It is understood that the Examiner has recognized that the previous amendment to claims 1 and 6 required that the bovine serum albumin (BSA) be fragmented, which feature was not present in the previously cited art, such as the Hunter et al reference. However, the Office Action asserted (at the top of page 4) that it would have been obvious to one of ordinary skill in the art to degrade BSA with pepsin to produce fragmented BSA based on Dosa et al reference. The same reasoning was applied to the rejection of claims 5 and 10 as set forth on page 5 of the Office Action, except that additionally the Nakase et al reference was relied upon as disclosing the addition of BSA to streptolysin O stabilizes streptolysin O and allows it to maintain its activity.

Applicants respectfully traverse the new rejections under 35 U.S.C. § 103(a). Particularly, based on an understanding of the details and implications of the present invention *vis-à-vis* the actual teachings of the Dosa et al reference in relationship to the other references, it will be seen that the presently claimed invention is unobvious and patentable over the cited references, and that a person of ordinary skill in the art would not arrive at the present invention based on a consideration of Dosa et al in combination with the other cited references.

(1) Mechanism of the present invention

In general, the surfaces of the latex particles are coated with an appropriate blocking agent such as bovine serum albumin (BSA) [see Example 2(1) of the present specification] to avoid a non-specific binding between the latex particles and a sample. When a sample contains an anti-BSA antibody, an unfavorable agglutination of latex particles is caused by an antigen-antibody reaction between the anti-BSA antibody and the BSA coated on the surfaces of the latex particles, regardless of the presence of a substance to be assayed, and thus, an accurate measured value cannot be obtained. In a conventional latex turbidimetry method, BSA is added to a reaction system to avoid such an influence of an anti-BSA antibody contained in a sample, because the anti-BSA antibody is absorbed by the BSA. However, there still remain samples showing a non-specific reaction which cannot be absorbed only by the addition of BSA. This was a problem to be solved by the present invention.

The present inventors newly found that a factor of the non-specific reaction is an antibody specific to BSA fragments contained in a sample. When BSA is immobilized on the surface of a latex particle, the conformation of the BSA is changed and internal epitopes embedded in the BSA are exposed. Such internal epitopes are not recognized by an anti-BSA antibody (i.e., an antibody prepared by using intact BSA as an immunogen), but are recognized by an antibody specific to BSA fragments (i.e., an antibody prepared by using BSA fragments as an immunogen). Part of the antibodies specific to BSA fragments can be absorbed, but all

antibodies specific to BSA fragments cannot be absorbed, only by the addition of BSA. All antibodies specific to BSA fragments can be absorbed by an addition of BSA fragments.

(2) The Dosa et al reference

As pointed out by the Examiner, Dosa et al discloses BSA fragments digested with pepsin, and the effect of peptic degradation on the immunological and antigenic properties of BSA. Dosa et al discloses that a pretreatment of mice with BSA fragments before immunization with intact BSA resulted in significant suppression of both the primary and secondary antibody response (see Summary).

This effect of BSA fragments disclosed in Dosa et al is a so-called "immunological tolerance" in which immunocytes are essentially involved, i.e., an effect in a living body. In contrast, the effect of BSA fragments found by the present inventors is an effect in an in vitro reaction system. Therefore, the technical field is quite different.

Furthermore, the finding that a factor of the non-specific reaction in a conventional latex turbidimetry method is an antibody specific to BSA fragments contained in a sample is not disclosed or suggested in Dosa et al. Therefore, Applicants submit that the use of BSA fragments in a latex turbidimetry method would not be motivated from Dosa et al.

In view of the above, reconsideration and allowance of claims 1, 4 - 6, 9 and 10 this application are now believed to be in order, and such actions are hereby earnestly solicited.

If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned attorney at the local Washington, D.C. telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

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